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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,081	10/24/2001	Avi J. Ashkenazi	GNE.2630P1C69	4135

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HELLER EHRMAN LLP  
275 MIDDLEFIELD ROAD  
MENLO PARK, CA 94025-3506

EXAMINER

LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/017,081	ASHKENAZI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 October 2001.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 58-77 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 58-77 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 October 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>4/30/02</u> . | 6) <input checked="" type="checkbox"/> Other: <u>Sequence Comparison A</u> .            |

*pd*

## **DETAILED ACTION**

### ***1. Formal Matters***

- A. The Preliminary Amendment dated 10/24/01, has been entered into the record.
- B. The Preliminary Amendment dated 9/3/02, has been entered into the record.
- C. Claims 58-77 are pending and are the subject of this Office Action.

### ***2. Information Disclosure Statement***

- A. References 1 and 2 on the IDS dated 4/30/02 have been lined through since they are not in proper format, including author and accession number.

### ***3. Specification***

- A. Though none could be found, due to the length of the specification, Applicants are reminded that embedded hyperlink and/or other form of browser-executable code are not permitted in the specification. See MPEP § 608.01.

- B. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title recites polypeptides and polynucleotides whereas the claims are drawn to polynucleotides.

### ***4. Claim Objections***

- A. The syntax of claims 58-77 could be improved by replacing the phrase “shown in Figure 79 (SEQ ID NO:216)” or “shown in Figure 78 (SEQ ID NO:215)” with “of SEQ ID NO:215.”

### ***5. Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

- A. The specification asserts that the protein tests positive in the following assays: Retinal Neuronal Survival (Assay #52); Rod Photoreceptor Survival (Assay #56) and Induction of Endothelial Cell Apoptosis (ELISA) (Assay 109). However, utility under 35 USC 101 is provided solely by Assay #109. However, as discussed below, the claims are not enabled.

**6. Claim Rejections - 35 USC § 112, first paragraph - enablement**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 58-77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The main issue to be considered is whether this assay is predictive of efficacy in treatment of retinal disorders associated with loss of rod photoreceptors. The specification has not demonstrated that the models used are art-accepted. The art-accepted models use systems in which the rod photoreceptors degenerate, similar to the disease situation giving significance to the increase in survival. See for example, Streichert LC, Birnbach CD, Reh TA., J Neurobiol. 1999 Jun 15;39(4):475-90 and Petters RM et al., Nat Biotechnol. 1997 Oct;15(10):965-70.

The instant specification does not provide any guidance or working examples of any art-accepted model in which to study disease situations. The instant assay only measures percent survival from a mixed population of first generation tissue culture cells. Given this lack of guidance and working examples of any art-accepted model which would be representative of any disease state desired to be explored, it is not predictable to the artisan that, respectfully, simply since a protein (e.g. PRO846) is positive in an assay using first generation tissue culture cells that it would be indicative of any successful treatment of any disorders requiring the survival of rod photoreceptor cells.

Furthermore, the specification only teaches that the protein is capable of enhancing the survival of rod photoreceptors and, therefore, that it is capable of treating various eye disorders. However, it is unclear how enhancing survival can treat a potentially large list of diseases. First, the specification does not disclose but a couple disorders which can potentially be treated, with no demonstration of any treatment being performed. Second, the specification only teaches that rod photoreceptor survival is

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increased. It does not state that these cells can be regenerated. It would be expected, in absence of evidence to the contrary, that many eye disorders occur from the lack of cells, or cell death. The protein of the invention has not been shown to regenerate or grow photoreceptor cells, simply to keep current ones from dying. This would not appear to be necessary to treat eye disorders since, if the photoreceptors were already present, increasing their survival would not affect the cells if they were properly functioning in the first place. Growth of new photoreceptors would be believed to be required. The specification does not demonstrate this.

B. Claims 58-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:215 and 216, does not reasonably provide enablement for polynucleotides or polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity to SEQ ID NO:215 or 216, to the protein encoded by ATCC No. 209847, for the extracellular domain thereof, or for vectors and host cells containing these polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. **There is no functional limitation in the claims, nor have Applicants taught which regions of the encoded polypeptide are required to maintain any function of this protein.** The claims encompass an unreasonable number of inoperative polypeptides, or polynucleotides which encode these polypeptides, which the skilled artisan would not know how to use.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

There are no working examples of polynucleotides or polypeptides less than 100% identical to SEQ ID NO:215 or 216, or the mature form thereof (i.e. lacking its signal peptide). The skilled artisan would not know how to use non-identical polypeptides or polynucleotides on the basis of teachings in the prior art or specification unless they possessed a specific function disclosed in the instant specification, in which there is none. While the specification generally describes homologous proteins, Applicants still have not taught to which family of proteins the protein of the present invention belongs. The specification does not provide guidance for using polynucleotides encoding polypeptides related to (i.e., 80%-99% identity) but not identical to SEQ ID NO:215 or 216 which do not have any specific, known function.

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The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitation.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the diversity of proteins and lack of knowledge about function(s) of encompassed polypeptides structurally related to SEQ ID NO:216, or their encoding polynucleotides (e.g. SEQ ID NO:215) the lack of direction or guidance for using polypeptides that are not identical to SEQ ID NO:216, and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

**7. Claim Rejections - 35 USC § 112, first paragraph – written description**

A. Claims 58-77 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to polynucleotides having at least 80%, 85%, 90%, 95% or 99% sequence identity with SEQ ID NO:215 as well as vectors and host cells. The claims do not require that the polynucleotides or encoded polypeptides of the present invention possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above,

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the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:216, or encoded by SEQ ID NO:215, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

#### **8. Claim Rejections - 35 USC § 112, second paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 58-77 are vague and indefinite since it is not clear whether or not the protein encoded by the polynucleotide of the present invention is a soluble protein (e.g. protease), nor is it disclosed as being expressed on a cell surface. Accordingly, the limitation that the claimed protein comprises an "extracellular domain" is indefinite, as the art does not recognize soluble proteins as having such domains. Further, if the protein had an extracellular domain, the recitation of "the extracellular domain"... "lacking its associated signal sequence" is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

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B. Claims 71-73 are vague and indefinite since the claim recites “hybridizes” without the recitation of any conditions, or recites “stringent conditions: wherein these conditions are not known. Nucleic acid molecules which hybridize under conditions of “low” stringency would not necessarily hybridize under conditions of “high” stringency. Furthermore, not all conditions of “high” or “low” stringency, for example, are the same. Therefore, it is required that Applicants amend the claims to recite the exact hybridization conditions without using indefinite phrases such as “*for example*” **without adding new matter.**

### ***9. Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 71-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al. (Accession No. U70073). The claims recite a polynucleotide which is at least 10 nucleotides in length and which hybridizes to SEQ ID NO:215. Jones teach a polynucleotide which is 20.5% identical to SEQ ID NO:215 and is 97.9% identical over 580 bases. This polynucleotide would be expected to hybridize even under the most stringent conditions (Sequence Comparison A).

### ***11. Conclusion***

A. No claim is allowable.



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***Advisory information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (571) 272-0888. The examiner can normally be reached on M-Th 10 AM – 7 PM (eastern); alt F 10 AM – 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert Landsman  
Primary Examiner  
Art Unit 1647

  
ROBERT S. LANDSMAN, PH.D.  
PRIMARY EXAMINER